Attorney Docket No.: 050623.00334

REMARKS

Claims 25, 30 – 32, and 34 were pending. Claims 25, 30 – 32, and 34 have been rejected. Claim 25 has been amended. Claims 35 – 43 have been newly added. Claims 25, 30 – 32, and 34 – 43 will be pending upon entry of this amendment.

No new matter has been added. New claims 35 – 38 are supported at least by page 4, lines 9 and 10, and page 30, lines 31 – 33 of the specification as filed on September 15, 2003. New claim 39 is supported at least by page 12, lines 20 and 21 of the specification. New claims 40 – 43 are supported at least by page 16, lines 11 – 20 of the specification.

Reconsideration is respectfully requested.

Claim Rejections - 35 U.S.C. § 103

The Examiner has rejected claims 25, 30 – 32 and 34 under 35 U.S.C. § 103(a) as being unpatentable over Hunter *et al.*, United States Patent No. 5,886,026 (Hunter).

The Examiner's Contentions

The Examiner contends that Applicants' claims are obvious in view of Hunter. According to the Examiner, Hunter teaches "methods for the preparation of drug-loaded microspheres, which are provided as a coating onto a stent, whereby the drug (i.e., paclitaxel) is dissolved in a polymer solution containing a polymer and solvent (DCM), and wherein the solvent is evaporated to yield microspheres." The Examiner also states that Hunter discloses numerous compositions including pastes "in the form of a suspension wherein the microspheres are suspended in a hydrophilic gel," and that among the methods of treatment disclosed in Hunter is one in which "the gel or paste can be smeared over tissue." The Examiner concludes with the statement that "[t]he methods of Hunter are useful and effective for the treatment of angiogenic-dependent diseases and thus would include restenosis, as is instantly claimed." In the Response to Arguments, the Examiner has stated that Applicants' arguments in the previously filed response are unpersuasive. The Examiner further elaborates by stating "the prior art's method of preparation yields an end result essentially the same as that desired in the instant invention," where "the end result being a layer containing particles of polymer combined with the therapeutic substance."

Applicants traverse.

Applicants' Response

First, without concurring in the Examiner's reasoning, the Examiner's comment that "the prior art's method of preparation yields an end result essentially the same as that desired in the instant invention" is irrelevant as Applicants' claims are directed to methods. Applicants are not claiming a product.

Second, Applicants are unable to identity where Hunter discloses a stent coating of microparticles. Example 9 discloses methods of coating stents with polymers such as polycaprolactone (PCL) including the operation of dissolving the polymer in a solvent, in this case, dicloromethane (DCM). Example 8 describes some methods of manufacturing microspheres that also involves dissolving PCL in DCM. It appears that the Examiner is assuming that since both processes involve dissolving the same polymer in the same solvent that microparticles are necessarily produced. If this is the Examiner's interpretation, the Examiner is mistaken because the processing steps differ. In Example 9 the solution is sprayed onto a stent or a stent is dipped into the solution, thus forming a coating on the stent. In Example 8, the polymer solution made using an organic solvent is added to an aqueous solution to form an emulsion from which particles are formed when the organic solvent is eventually evaporated. Thus, the process of Example 9 does not produce microparticles.

Third, the Examiner has not established a *prima facie* case of obviousness. The Supreme Court has recently stated:

> a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

KSR International Co. v. Teleflex Inc. et al., 127 S. Ct. 1727, 1741 (2007) (emphasis added). Although Applicants recognize that this precedent also holds that there need not be a specific teaching, suggestion or motivation in the art, "rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with

some rational underpinning to support the legal conclusion of obviousness." *Id.* (citations omitted)(emphasis added).

In the present case, the Examiner has cited elements that are, in the Examiner's view, taught by Hunter. However, the Examiner has provided no reason to explain why one of skill in the art would have combined the elements to yield Applicants' claimed invention. The Examiner has merely made the conclusory statement that "[t]he instant invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made given the teachings of Hunter." The Examiner then proceeds to summarize what the Examiner interprets to be the teachings of Hunter. Applicants submit that such discussion is not "articulated reasoning with some rational underpinning."

Fourth, based upon the disclosure of Hunter, one of skill in the art would not have been motivated to combine the various elements in Hunter in a manner that would have resulted in the Applicants' claimed invention. It appears, based on Applicants' understanding of the Examiner's rejection, that the Examiner is relying upon Hunter's disclosure of nanospray and nanopaste formulations to support the conclusion of obviousness. The nanospray formulation discussed in Example 10 (B) beginning at column 49, line 54 is a "suspension of small microspheres in saline." The suspension is intended for "deposition onto tissue through a finger pumped aerosol." (column 49, lines 60 and 61) The nanopaste is described in Example 10 (E) as "a suspension of microspheres suspended in a hydrophilic gel." (column 52, lines 61 and 62) The paste may be "smeared over tissue." (column 52, line 62) The paste is "diluted with bodily fluids causing a decrease in the stickiness of the paste and a tendency of the microspheres to be deposited on nearby tissue." (column 52, line 64 – column 52, line 1) Example 20 also discloses a suspension of microparticles in a solution for ophthalmic use. (column 67, lines 19 – 49)

The use of a suspension as a pharmaceutical formulation would not have led one to have used a suspension of microparticles in a coating material that "includes a polymeric material dissolved in a solvent." First, disclosure of suspensions which are formulations for drug products would not have led one to have used a suspension as an intermediate for processing. Second, in all of the above cited instances of suspensions disclosed in Hunter, the microparticles in suspension are in a "carrier," such as saline or the hydrophilic gel, which is used to deliver the microparticles to the tissue. After the microparticles are delivered to the tissue, the carrier essentially disappears, leaving only the microparticles. In contrast, Applicants' claims specify

that the microparticles are suspended in a coating material that "includes a polymeric material dissolved in a solvent," and results in the microparticles becoming embedded in or attached to a film of the polymeric material once the suspension is applied to a stent and the solvent has evaporated. Therefore, the above cited suspensions in Hunter would not have led one to have formulated the suspension of Applicants' claims and to have used it in the manner specified by Applicants' claimed methods. Clearly the Examiner is relying upon hindsight knowledge of Applicants' invention in concluding that Applicants' claims are obvious by interpreting the disclosure of a drug product that is a suspension as reading on Applicants' claimed suspension which is a different suspension and is used for a different purpose.

Fifth, Hunter teaches away from including microparticles in a stent coating, or in other words, Hunter teaches away from the claimed invention. The Federal Circuit recently reiterated the test for teaching away from the invention:

> A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *In re Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994); see KSR, 127 S. Ct. at 1739-40*

In re Icon Health and Fitness, Inc., 496 F.3d 1374, 1381; 83 U.S.P.Q.2D 1746 (Fed. Cir., 2007) (emphasis added). In determining obviousness, a reference that teaches away from the claimed invention is a "significant factor" to be considered. Manual of Patent Examining Procedure, § 2145(d)(1).

With respect to stent coatings, Hunter states that "it [the anti-angiogenic composition] should preferably coat the stent smoothly and evenly, with a uniform distribution of angiogenesis inhibitor, while not changing the stent contour." (column 22, line 66 – column 23, line 2) Upon reading the above statements in Hunter, one of skill in the art would not have been led to include microparticles in a stent coating as the therapeutic substance would not be uniformly distributed. Moreover, a coating including microparticles may not provide a smooth and even coating.

In summary, for all of the reasons discussed above, claim 25, and thus also claims that depend from claim 25, are not rendered obvious by Hunter. Applicants respectfully request the withdrawal of the obviousness rejection.

Patentability of New Claims

New claims 35 – 43 depend from claim 25, either directly or indirectly, and are therefore patentable over Hunter for at least the same reasons that claim 25 is patentable over Hunter. In addition, claims 35 – 38 recite polymers that are not among those listed as "polymeric carriers" in Hunter. Thus, there is an additional reason for the patentability of new claims 35 – 38.

Conclusion

In light of the foregoing claim amendments and remarks, this application is considered to be in condition for allowance. Applicants respectfully request the allowance of pending claims 25, 30 – 32, and 34 – 43.

If necessary to ensure a timely response, this paper should be considered as a petition for an Extension of Time sufficient to provide a timely response. The undersigned authorizes the Commissioner to charge any fees that may be required, or credit any overpayment to be made, to the **Squire, Sanders, and Dempsey Deposit Account No. 07-1850**.

Should the Examiner have any questions regarding this communication, the Examiner is invited to contact the undersigned at the telephone number shown below.

Respectfully submitted,

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